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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,467	12/04/2001	Keith D. Allen	R-758	7217

26619 7590 11/21/2006

JOHN E. BURKE
GREENBERG TRAURIG LLP
1200 17TH STREET, SUITE 2400
DENVER, CO 80202

EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/21/2006

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/005,467
Filing Date: December 04, 2001
Appellant(s): ALLEN, KEITH D.

John Burke
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed on 3/30/06 appealing from the Office action mailed on 3/22/05.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows:

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner.

The rejection of claims 28-32, 37, 47, 52-54 and 57 under 35 U.S.C. 112 1st paragraph (new matter) is withdrawn in light of Appellant's amendment.

The rejection of claim 32 under 35 U.S.C. 112 2nd paragraph is withdrawn in light of Appellant's amendment.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Ogata et al., 1998. Journal of Biological Chemistry. Vol. 274, No. 18, pp. 12905-12909.

Sigmund, C.D., 2000. Arterioscler Thromb Vasc Biol.20:1425-1429.

Wall, R.J., 1996. Theriogenology 45:57-68.

Jacks et al., 1992. Nature, Vol 359, pp. 295-300.

Olsen 2000. GABA in the Nervous System, pp. 81-95.

Elchebly et al., 1999. Science Vol 283:1544.

http://www.mercksource.com

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 101 and 112 1st paragraph

Claims 28-32, 37, 47, 53-57 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, substantial and specific asserted utility or a well established utility.

The claims are drawn to a transgenic mouse whose genome comprises a null allele in the endogenous PTP36 gene (28, 53-57). The claims are also drawn to female homozygous PTP36

knockout mouse displays one of the following phenotype: uterine dilation, keratin in the uterine horns or lumen, increased liver weight, increased spleen weight, increased thymus weight, increased liver weight relative to body weight, increased spleen weight relative to body weight (29-32). The claims are further drawn to a method of making said mouse, and cells and tissues isolated from said mouse (37).

No well-established utility exists for the claimed transgenic mouse. However, the specification asserts or implies the following as credible, specific and substantial patentable utilities for the claimed transgenic knockout mouse and cells or tissues isolated from said mouse:

1) To be used in methods of identifying agents capable of affecting a phenotype of said mouse.

2) To identify agents useful as therapeutic agents for treating conditions associated with a disruption or other mutation of the PTP36 gene.

3) To identify agents having an effect on PTP36 expression or function.

4) To test and develop new treatments relating to the behavioral phenotypes.

Each of the following shall be addressed in turn:

1) To be used in methods of identifying agents capable of affecting a phenotype of said mouse. This utility is not substantial because the specification does not disclose a utility for such agents. In other words, why would a skilled artisan wish to identify such agents? The prior art (Ogata et al., 1998, from IDS) teaches PTP36 is involved in the regulation of cell adhesion, cell growth and cytoskeleton in Hela cells. However, it is not known to be associated with any disorder that have the symptom of increased liver, spleen, thymus weight or uterine dilation, presence of keratin in the uterine horns or lumen. The disclosed phenotype of the instantly

claimed mouse, increased liver, spleen, thymus weight, or uterine abnormality (in female mice only) do not correlate with the hypothesized function of PTP36 in focal adhesion. Although the agents can affect a phenotype in said transgenic mouse or a cell/tissue isolated from said mouse, the utility is not substantial because there is no other use of said agents except affecting a phenotype that only exists in a mouse. Since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not credible, specific or substantial.

2) To identify agents useful as therapeutic agents for treating conditions associated with a disruption or other mutation of the PTP36 gene. This utility is not credible and specific because the specification does not disclose what kind of conditions is associated with a disruption or other mutations of the PTP36gene. The specification also fails to teach what specific condition is associated with the overall phenotype of uterine abnormality comprising keratin in the uterine horn or lumen, increased organ weight. The art does not recognize any disorders that are associated with the overall phenotype of increased liver, spleen, thymus weight, uterine dilation and presence of keratin in the uterine horns and lumen. As such, the claimed mouse is not a valid model for any disorder. Since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not credible, specific and substantial.

3) To identify agents having an effect on PTP36 expression or function. This asserted utility is not credible or substantial because the specification does not disclose 1) how to use a mouse or cell that does not express PTP36 to identify agents which affect the gene expression or function; 2) how to use a heterozygous PTP36 knockout mouse to identity agents which affect

the gene expression or function; 3) how to use such identified agents that affect PTP36 expression or function. This asserted utility is not credible since there is no expression or function can be monitored in the knockout mouse or cells/tissues isolated from said mouse, it is unclear how these agents that affect PTP36 expression/function can be identified. Claims 28, 37, 53, 55-57 encompass heterozygous knockout mouse. The heterozygous knockout mice usually have no difference in expression relative to a wild type mice. As such, a skilled artisan would not know how to use a heterozygous PTP36 knockout mouse to identify agents that have an affect on PTP36 expression. Further, the specification does not teach any use for the agents that have an effect on PTP36 expression or function. Since the identified agents do not have a substantial utility, the claimed mouse or mouse cells used in a method for identifying such agents does not have substantial utility as well.

4) To test and develop new treatments relating to the behavioral phenotypes. This utility is not credible, substantial and specific because the specification does not teach that the claimed mouse displays any behavioral abnormality. As such, it is not a valid model for any behavioral disorder. Since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not credible, specific or substantial.

Since the claimed transgenic mouse and cells/tissues isolated from said mouse does not have utility, the method for producing said transgenic mouse does not have utility either. Therefore, the claimed invention lacks patentable utility for reasons given above.

Claims 28-32, 37, 47, 52-54 and 57 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible,

substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, even if the claimed mouse has utility, it would require undue experimentation to make and use the invention as claimed.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the Invention:

Claims 28-32, 37, 47, 53-57 are drawn a transgenic mouse whose genome comprises a null allele in the endogenous PTP36 gene, wherein the null allele comprises a neo-lacZ selection marker, wherein the disruption is homozygous, the mouse exhibits phenotype of increased liver, spleen, thymus weight, wherein the female mouse exhibits uterine dilation, presence of keratin in uterine horns and lumen. The claims are further drawn to a cell or a tissue isolated from said transgenic mouse, and a method of producing said transgenic mouse.

Breadth of claims and amount of guidance in the specification and working Examples:

In the instant case, claims 28-32, 37, 47, 53-57 encompasses a transgenic mouse that comprises a null allele in the endogenous PTP36 gene. The specification does not provide an

enabling disclosure for how to use the transgenic mouse as claimed. The specification discloses a PTP36 transgenic knockout mouse, wherein the disruption is homozygous, the mouse exhibits phenotype of increased liver, spleen, thymus weight, wherein the female mouse exhibits uterine dilation, presence of keratin in uterine horns and lumen. The specification does not provide specific teaching on how to use these mice with the disclosed phenotype. The specification prophetically teaches that the transgenic mouse can be used to screen drugs or as models for diseases, or screening agents that modulates a phenotype of said mouse. However, the specification fails to teach what type of diseases are the disclosed phenotypes related to. The specification also fails to teach how to use the agent that modulates the phenotype associated with PTP36 gene disruption. As such, one skilled in the art would not know how to use the transgenic mouse with the phenotype of increased liver weight, for example, as a disease model or screen drugs for a specific disease. Moreover, the specification fails to teach how to use a cell or tissue isolated from the transgenic mouse. Therefore, the teaching of the specification is limited.

The state of art and the predictability in the art

The state of art at the time of the filing is silent on a transgenic mouse whose genome comprises a null allele in the endogenous PTP36 gene, wherein the disruption is homozygous, the mouse exhibits phenotype of increased liver, spleen, thymus weight, wherein the female mouse exhibits uterine dilation, presence of keratin in uterine horns and lumen, as compared to a wild type mouse. At the time of filing, the function of the PTP36 gene is unclear. *In vitro* experiments demonstrate that (Ogata et al.) over-expression of the murine PTP36 in Hela cells renders the cells to spread less well, grow more slowly and adhere to the extracellular matrix

protein less well, which suggests that PTP36 is involved in the regulation of cell adhesion, cell growth and cytoskeleton process. However, the art does not provide any teaching regarding the relationship between PTP36 function and the disclosed phenotype. The overall phenotype observed in the claimed mouse does not correlate to the hypothesized function of PTP36 which is involved in cell adhesion and cell growth. As such, whether the claimed mouse can be used as a model to study PTP36 in the process of cell adhesion and cell growth is unpredictable.

At the time of filing, the phenotype of the transgenic knockout mouse is considered unpredictable. One has to remember that many of the phenotypes examined in transgenic and knockout models are influenced by the genetic background in which they are studied and the effect of allelic variation and the interaction between the allelic variants (pg.1425, paragraph 1 in Sigmund, C.D. 2000. Arterioscler Thromb Vasc Biol.20:1425-1429). Further, the transgene expression and the physiological consequences of transgene products are not always accurately predicted in transgenic mouse studies (pg.62, paragraph1, lines 7-9 in Wall, R.J. 1996. Theriogenology 45:57-68). The particular genetic elements required for expression varies from species to species. Our lack of understanding of essential genetic control elements makes it difficult to design transgenes with predictable behavior (Wall, 1996). For example, Jacks et al. (1992) describe Rb knockout mice that do not display retinoblastoma; rather they exhibit the unexpected phenotype of pituitary tumors. The pituitary tumors arise from cells lacking a wild-type Rb allele. Thus, tumors were found to arise not in retinas, as in humans, but in the pituitary gland (page 299, Discussion, paragraphs 1 and 3). In the instant case, the function of the PTP36 *in vitro* is not predictive of its function *in vivo*. Thus, one skilled in the art would not know how

to use the claimed mouse with no phenotype (such as a heterozygote), or the phenotype which is independent of the transgene function.

The specification teaches that the claimed mouse can be used as disease models and used for screening drugs. However, a search of the prior art does not reveal any known disease which is correlated with the disclosed phenotypes. The mere statement from the specification that the mouse can be used as a disease model is so vague which renders it meaningless as a specific teaching for how to use said mouse. Without any guidance from the specification, one skilled in the art would engage in undue experimentation to determine how to use the claimed mouse for the disclosed embodiments. Therefore, the instant specification fails to enable the PTP36 knockout mouse as claimed.

(10) Response to Argument

The examiner has responded to Appellant's argument presented in the Appeal Brief in the office action mailed on 2/13/06. In the Reply Brief filed on 3/22/06, Applicant made additional arguments in response to examiner's answer, and they are addressed as following.

Appellant argue that the specification teaches the claimed mice demonstrated androgenization on page 49, lines 14-23. However, as discussed in the previous examiner's answer, the cited paragraph only teaches that female homozygous PTP36 knockout mouse displays the phenotype of lack of mammary tissue, presence of keratin in the uterine horn and lumen, and such phenotype suggests a hormonal imbalance, which is consistent of androgenization. However, the specification does not assert any use based on the observed phenotype. The term "androgenization" means a process of showing effects to androgen, which also means musculinization (defined by Mercksource.com). It further explains that it is a process

of 1. the normal development of primary or secondary sex characters in the male. 2. the induction or development of male secondary sex characters in the female or prepubertal male, such as enlargement of the clitoris or penis, growth of facial and body hair, and deepening of the voice. 3. the condition of having such sex characters. The prior art teaches that clinical symptoms of hyperandrogenism in female include hirsutism, seborrhea, acne, hair loss, clitoridean hypertrophism, voice alteration, mammary hypertrophism and muscular growth (see cited references, Exhibit Q and R). The overall phenotype of the claimed female mouse does not reflect such symptoms that are demonstrated in the human hyperadrogenism. The specification also fails to disclose whether female mice having "androgenization" phenotype actually have altered male/female sex hormone level. Furthermore, if the PTP36 is involved in the androgenization process, it would also have produce androgenic effect in male mouse as well. Moreover, Appellants assert that hyperandrogenism is a condition may ultimately lead to life-threatening cardiovascular problems and metabolic disorder (see page 2 or the Reply Brief). The instant specification does not demonstrate any mouse having hyperandrogenism that has a cardiovascular or metabolic disorder. The specification fails to teach what role PTP36 plays in the androgenization process except that female mice lack PTP36 expression lack mammary gland tissue, increased anogenital distance and producing keratin in uterine horn and lumen, wherein the overall phenotype has not been found in human hyperandrogenism. In other words, the specification fails to establish the nexus between androgenization and the observed phenotype, hence the function of PTP36 in androgenization process. The prior art does not teach human hyperandrogenism is correlated with the loss of function of PTP36 gene. Therefore, combining the teaching of the instant specification and information that is readily available in the

prior art, one skilled in the art would not be able to use the claimed mouse as a model to study androgenization without undue experimentation. Thus, the alleged use of the claimed mouse to study androgenization is not a well-established use because a person of ordinary skill in the art would not immediately appreciate why the invention is useful based on the characteristics of the invention. Therefore, since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not credible, specific or substantial.

Appellant further cited specification from page 3-4 and page 17 to demonstrate that the specification discloses 1) how to use a mouse or cell that does not express PTP36 to identify agents; 2) how to use a heterozygous PTP36 knockout mouse to identify agents and for PTP36 expression analysis; and 3) how to use identified agents to treat diseases and conditions associated with gene expression or disruption. This argument is not persuasive because the teaching provided in the cited passage is directed to generic use of any transgenic knockout mouse, not for specifically to the PTP36 knockout mouse. In other words, it does not provide a substantial and specific utility for the claimed PTP36 knockout mouse (for detailed discussion, see pages 11-15 of the examiner's answer).

Appellant argues that the hitchhiker effect discussed by Sigmund is a rare phenomena citing Wolfer et al. Appellant further asserts that the specification discloses that the knockout mice were generated following guidelines set by Sigmund with appropriate controls citing Example 1. In response to Appellant's argument regarding Sigmund, the examiner would like to point out that the problem discussed in the article is not limited to "hitchhiker effect," which is referring to the observed phenotype resulting from genes linked to targeted gene rather than null mutation. Sigmund reference also discusses phenotypes of transgenic and knockout models are

influenced by genetic background in which they are studied, and such genetic background is the collection of all genes present in an organism that influences a trait or traits. Sigmund indicates that "these epigenetic effects can dramatically alter the observed phenotype and therefore can influence or alter conclusions drawn from experiments" and listed examples in the Table on page 1426. Sigmund assert that "studies performed over the past few years have clearly illustrated that phenotypes caused by specific genetic modification are strongly influenced by genes unlinked to the target locus (see page 1425 1st col., 1st-2nd paragraph). This aspect is also discussed in Wolfer et al. on page 336, 3rd col. Wolfer et al. assert that "anther possible complication with in gene knockout experiments is the fact that the phenotype resulting from a null mutation can depend on the general genetic background of mouse strains used for this research, and congenic strains carrying the same null mutation can sometimes show widely divergent phenotypes depending on the genotype of the recipient strain." With regard to the "hitch-hiker" effect, although Wolfer et al. does indicate that the statistically expected number of confounding flanking genes is relatively low, the reference also states that "however, active search for flanking gene effects has indeed revealed candidate cases (citing Kelly, Bolivar and Gerlai references)" (see page 336, 2nd col., the sentence following the cited paragraph). As such, the references cited by both examiner and Appellant support the notion that the phenotype of the transgenic knockout mouse is unpredictable at the time of filing. In response to Appellant's assertion that the specification discloses that the mice were generated following guidelines set by Sigmund, the examiner respectfully disagrees. Sigmund teaches the generation of congenic strains to generate homogeneous genetic background (see page 1427, bridging paragraph) and examining large number of mice to ensure the range of phenotype possible due to epigenetic

interaction is observed in the instance that a congenic strain has not been generated (see page 1428 2nd paragraph). The specification (Example 1) only discloses "ES cells derived from the 129/OlaHsd mouse substrain were used to generate chimeric mice. F1 mice were generated by breeding with C57BL/6 females. F2 mutant were produced by intercrossing F1 heterozygous males and females...Wide type control mice, as well as heterozygous and homozygous mutant mice were evaluated by the following experiments or tests." In this cited paragraph from Example 1, there is no information with regard to what strain of mouse is used to generate chimeric mouse, how many backcross is conducted to generate congenic strains (Sigmund states that 6 generation of backcross breeding is required before the genetic backgrounds are statistically >99% homogenous), whether speed-congenic approach is used, or how many control and mutant mice were used in each experiment, except that 3 homozygous female mutant were used with the age and gender matched control in assessing body and organ weights. As such, it is unclear whether the specification followed the guidelines suggested by Sigmund to minimizing background effect.

Appellant alleges that the examiner cited Wall reference out of context because Wall discusses issues associated with expression of transgenes in livestock and that experimentation should take in species of interest. Appellant asserts that the claim is drawn to a knockout mouse, not a transgenic livestock; therefore, Wall is not relevant to the claimed invention. Appellant further alleges that Jacks fails to support the position that knockout mice phenotypes are unpredictable because mice lacking Rb does develop tumor in pituitary, thus indicate its association with tumor growth. Therefore, one skilled in the art would accept that PTP36 gene is

involved in sexual development and fertility because the PTP36 knockout mouse demonstrates androgenization phenotype.

The examiner respectively disagrees the above assertion. Wall reference addresses the phenomena that transgenic phenotype in livestock is not accurately predicted in transgenic mouse studies, indicating the phenotype of a transgenic animal varies from species to species. Although the instant claims are directed to a knockout mouse, it is also considered to be a transgenic mouse because null allele is generated by introducing exogenous genetic material into the mouse genome. The difference is whether the observed phenotype is due to the expression of a foreign gene or the lack of expression of an endogenous gene. Combining with the observation that lack of Rb expression in mouse, a phenotype observed in human associated with retinoblastoma, does not result in retinoblastoma, the prior art teaches that the transgene or knockout phenotype varies from species to species. Both these references support this notion. As such, the observed androgenization phenotype in the PTP36 knockout mouse by itself does not enable one skilled in the art to use said mouse as a model to study human androgenization. Although PTP36 may be involved in the sexual development and fertility, further experimentation is required to determine how to use said knockout mouse according to the disclosed embodiment.

Appellant further cited the following NIH press release to demonstrate the utility of the claimed mouse:

BETHESDA, Md., Wed., Oct. 5, 2005 - The National Institutes of Health (NIH) today announced contracts that will give researchers unprecedented access to two private collections of knockout mice, providing valuable models for the study of human disease and laying the groundwork for a public, genome-wide library of knockout mice.

Under terms of three-year contracts jointly funded by 19 NIH institutes, centers and offices, Deltagen Inc. of San Carlos, Calif., and Lexicon Genetics incorporated of The

Woodlands, Texas will provide NIH and its scientific partners with access to extensively characterized lines of mice in which a specific gene has been disrupted, or "knocked out." In the first year of the contract, NIH will expend about $10 million to acquire about 250 lines of knockout mice.

For each mouse line, the contractors will provide not only the mouse line itself, but also detailed, objective data on the impact of the specific gene deletion on the mouse's phenotype, which includes appearance, health, fitness, behaviour, ability to reproduce, and radiological and microscopic data. Such comprehensive information on such a large group of mice has never been available to public sector researchers, and is expected to greatly accelerate efforts to explore gene functions in health and disease. "Our decision to procure these knockout mouse lines and data and make them available to the research community will yield tremendous benefits, both in the short and long terms," said NIH Director Elias A. Zerhouni, M.D. "This trans-NIH initiative will place important mouse models into the hands of researchers, speeding advances in the understanding of human disease and the development of new therapies. It also represents a significant step in the direction of launching an international project to systematically knock out all genes in the mouse."

Since the early 1980s, when recombinant DNA technology was used to create the first such animals, knockout mice have proven to be one of the most powerful tools available to study the function of genes and to create mouse models of human disease. Researchers have produced knockout mice with characteristics similar to humans suffering from a wide range of disorders, including cancer, heart disease, neurological disorders and even obesity.

Appellant assert that the claimed invention is one of 750 lines of mice contained within Deltagen's Deltabase collection, which is under contract for NIH to have a three year option to obtain access approximately 125 lines of these mice. However, the claimed mouse has not been chosen yet. Appellant assert that NIH would not have expended public funds if they do not believe that the phenotypes were a result of the disruption.

In response to above arguments, the examiner would point out that while the NIH report suggests knockout mice may be models of disease, the specification does not provide evidence that mice with uterine dilation, the appearance of keratin in the uterine horn and lumen, increased organ weight, lack of mammary tissue, or presence of keratin in the uterine horn and lumen as claimed are models of any human disease. Furthermore, the above press release addresses the contribution of knockout mice and collective information as a whole to the research of human

disease because it is the "unprecedented access to two private **collection of knockout mice,** providing valuable models for the study of human disease," and "Such **comprehensive information** on such a large group of mice has never been available to public sector researchers, and is expected to greatly accelerate efforts to explore gene functions in the health and disease..." Moreover, Appellant has admitted that the claimed mouse is not among the 125 lines which have been acquired. As such, the above press release does not provide a substantial and specific utility for the claimed PTP36 knockout mouse.

Appellant further asserts that NIH, Merck, Pfizer and GlaxoSmithKline have spent more than sixty million dollars to access Deltagen's Delta base, and each mouse in the database is purchased by one of the companies. Appellant argues that this would indicate the method used by Deltagen is reliable in creating the knockout mice.

In response to this argument, the examiner would like to point out that even the data provided in Deltabase is reliable, the disclosure of the specification is insufficient to enable one skilled in the art to use the claimed PTP36 knockout mouse as a disease model. The examiner would also reiterate that using the claimed mouse to study the function of the PTP36 for a research use and an assessment that focuses on whether an invention is useful only in a research setting does not address whether the invention is in fact "useful" in a patent sense (see page 19 of Examiner's Answer). The Appellant provides no information with regard how the pharmaceutical company is going to use the claimed PTP36 knockout mouse. Since the claimed mouse is not among the 125 lines selected by NIH, it is unclear how NIH would use the claimed mouse either. The pharmaceutical company may purchase the claimed mouse to conduct basic research, however, such use does not constitute a patentable utility for the claimed mouse for

reasons discussed in the Examiner's Answer mailed on 2/13/06. With regard to the use of the claimed mouse for human therapeutic drug development, the specification fails to provide sufficient information to enable one skill in the art to use the claimed mouse for this purpose. The information contained in Deltabase or acquired by the pharmaceutical company is not fully disclosed in the instant specification. Based on the disclosure of the instant specification and the information from the prior art, one of skilled in the art would not know what specific disease the mouse model represents. Thus, it is unclear how this mouse can be used to develop human therapeutic drug, i.e. what type of disease the identified agent can treat. Absent evidence from the contrary, a general statement of development of human therapeutic drug, without specify which disease can be treated, is insufficient to support the enablement of such use. Therefore, the fact that the mouse is purchased by a large pharmaceutical company such as Merck, does not enable one of skilled in the art to use the claimed PTP36 knockout mouse as an animal model for a human disease.

In response to Appellant's argument that post filing evidence including NIH report and Austin should be considered by the examiner as evidence supporting the utility of the claimed invention, the examiner would like to point out that the above references have already been considered in the Examiner's Answer mailed on 2/13/06.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Celine Qian, 8/24/06

CELINE QIAN, PH.D.
PRIMARY EXAMINER

Conferees: